REMARKS

Claims 21, 24, and 31-38 are currently under examination. Upon entry of the above amendments, Claims 21, 24, 31, 33-38 will be under examination. Claim 32 has been canceled without prejudice. Claims 21, 24, 31, 33, and 34 have been amended. The amendments to claims 21, 24, 31 and 34 can be found in the specification at, *e.g.*, page 17, line 33, to page 18, line 2. The amendments to claim 33 can be found in the specification at, *e.g.*, page 17, line 33, to page 18, line 2, and page 17, lines 8-17. No new matter has been introduced.

Applicants respectfully submit that claim 30 has been incorrectly withdrawn from further consideration as it directs to elected subject matter. Claim 30 reads as "The nucleic acid molecule of claim 21 comprising SEQ ID NO: 99, nucleotides 3-1149 of SEQ ID NO: 101, ***nucleotides 123-1029 of SEQ ID NO: 103***, nucleotides 1-2266 of SEQ ID NO: 105, nucleotides 11-2308 of SEQ ID NO: 107, SEQ ID NO: 109, nucleotides 117-2382 of SEQ ID NO: 111, or nucleotides 117-2382 of SEQ ID NO: 113" (emphasis added). "Nucleotide 123-1029 of SEQ ID NO: 103" encodes SEQ ID NO: 104, and directly reads on the elected subject matter. As such, Applicants respectfully request that claim 30 be further examined.

1. Rejection Under 35 U.S.C. § 112, First Paragraph, Written Description, Should Be Withdrawn

Claims 32 and 33 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner contends that the Applicants have failed to provide a written description of the substitutions and deletions that would provide adequate support of the claims 32 and 33. Moreover, according to the Examiner, claims 32 and 33 are drawn to a genus of polypeptides that is defined by an unclear functional relationship to a nucleic acid molecule encoded polypeptide comprising the amino acid sequence of SEQ ID NO: 104.

Merely to expedite prosecution, claim 32 has been canceled without prejudice. Claim 33 has been amended to direct to an isolated nucleic acid molecule comprising an open reading frame encoding an amino acid sequence that is at lease 95% identical to SEQ ID NO: 104. As

such, the rejection under 35 U.S.C. § 112, first paragraph for written description, has been obviated, and should be withdrawn.

2. Rejection Under 35 U.S.C. §§ 101 and 112, First Paragraph, Should Be Withdrawn

Claims 21, 24 and 31-38 are rejected under 35 U.S.C. §101 for not being supported by either specific and substantial asserted utility or well-established utility. In particular, the Examiner contends that the utilities taught in the specification are not specific or substantial for either the nucleic acid molecule or protein. According to the Examiner, the NOV9d polypeptide encoded by the nucleic acid sequences of the invention (1) "has not shown to have primary structural similarity with the polypeptide encoded by polynucleotides that encode LIV 1 human protein, or any other polypeptide that exhibits such characteristics" (Office Action at page 10, lines 4-9); and (2) is not correlated with any disease or disorder.

Applicants respectfully disagree. Firstly, Applicants have clearly shown that NOV9d share primary structural similarity with the LIV-1 human protein. As well-known in the art, a protein's primary structure is simply the order of its amino acids (see, *e.g.*, Molecular Biology of the Cell, 2nd Edition, Alberts *et al.* ed., Garland Plublishing, Inc., (1989), page 112, lines 13-14). The instant application teaches that NOV9 sequences share high homology to LIV-1 protein (see, *e.g.*, Example 9, pages 116-127). By providing the sequence of NOV9d, it is also apparent to a skilled person in the art that NOV9d is a splice variant of LIV-1 simply by performing a sequence alignment of the two genes.

Secondly, Applicants respectfully submit that the instant specification teaches a specific, substantial and credible utility of the claimed nucleic acids for differentiating certain breast cancer cells from corresponding normal tissues. For example, the specification at, *e.g.*, page 50, line 33, to page 54, line 6, teaches how to detect the presence or absence of the claimed nucleic acids in a biological sample. Example 9 (pages 116-127) teaches that NOV9 family of genes is highly homologous to LIV-1, which is known to be highly expressed in certain breast cancer (see, *e.g.*, McClelland et al., Br. J. Cancer 77(10): 1653-1656 (1998) "Oestrogen-regulated genes in breast cancer: association of pLIV-1 with response to endocrine therapy"). The instant

application at pages 185-194 gives a working example and clearly shows that a nucleic acid sequence encoding a member of NOV9, NOV9a, is overexpressed in certain breast cancer cells as compared to corresponding normal tissue (see, *e.g.*, panels 1.3D, 2.2, and 2D). Therefore, the specification teaches how to use the claimed nucleic acids to differentiate certain breast cancer cells from normal breast tissue.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C § 101 be withdrawn.

Claims 21, 24 and 31-38 are also rejected under 35 U.S.C. §112, first paragraph, for not being supported by either a specific and substantial asserted utility or a well established utility. Applicants have demonstrated above that the pending claims are supported by a specific, substantial, and credible utility. Therefore, this rejection should be withdrawn.

3. Rejection Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn

Claims 21, 24 and 31-38 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which are not described in the specification in such a way as to reasonably convey to a skilled artisan that the inventor, at the time of filing of the application, had possession of the claimed invention. In particular, the Examiner states that the claims as presented encompass genomic DNA, which is not described in the specification.

Applicants respectfully disagree. However, merely to expedite prosecution, claims 21, 24, 31 and 33 (and claims depending thereon) have been amended to recite an isolated nucleic acid molecule comprising an open reading frame encoding an amino acid sequence of SEQ ID NO:104. As commonly understood in the art, a genomic DNA with one or more introns is not encompassed by claims as amended. As such, Applicants respectfully request the written description rejection be withdrawn.

4. Rejection Under 35 U.S.C. § 102(e) Should Be Withdrawn

Claims 21, 24 and 31-38 are rejected under 35 U.S.C. §102(e) as being anticipated by Mack et al., US Patent No. 6,752,020 ("the '020 patent"). According to the Examiner, the '020

patent discloses nucleic acid molecules that encode an amino acid sequence that comprises the amino acid sequence of SEQ ID NO: 104 (column 51-54, SEQ ID NO:4, nucleotides 1-357 and 1716-2265; column 47-48, SEQ ID NO:1, nucleotides 138-494 and 1853-2404).

Applicants respectfully disagree. The '020 patent discloses BCR4 gene (SEQ ID NO:5, which is encoded by SEQ ID NO: 1 or 4, see '020 patent, column 3, line 58, to column 4, line 22, and FIGs. 1-3). As shown in Appendix A (attached hereto), SEQ ID NO: 104 of instant application is a splice variant of BCR4. It is apparent that SEQ ID NO: 104 is not identical to BCR4. Nowhere in the '020 patent teaches SEQ ID NO:104 or how to obtain SEQ ID NO: 104 from BCR4 gene information. Even acknowledging high skill in molecular biology art, prediction of a splice variant of BCR4, SEQ ID NO: 104 of the instant invention, is highly unlikely based on the information provided in the '020 patent.

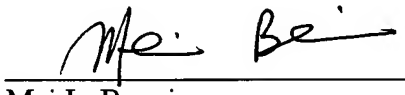
In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 102(e) be withdrawn.

CONCLUSION

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the present application. Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

Date: July 11, 2005



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Enclosures

Appendix A: ClustalW Alignment of SEQ ID NO:5 of US Pat. No. 6,762,020 (SEQ5P672020) and SEQ ID NO: 104 of present invention (CG56008-04)

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SEQ5P6762020    1 MARKLSVILILTFALSVTNPLHELKAAAFPQTTEKISPNWESGINVDLAISTRQYHLQQL  60
CG56008-04      1 MARKLSVILILTFALSVTNPLHELKAAAFPQTTEKISPNWESGINVDLAISTRQYHLQQL  60

SEQ5P6762020   61 FYRYGENNSLSVEGFRKLLQNIGIDKIKRIHIHHDHDHHSDHEHHSDHERHSDHEHHSDH 120
CG56008-04     61 FYRYGENNSLSVEGFRKLLQNIGIDKIKRIHIHHDHDHHSDHEHHSDHERHSDHEHH--- 117

SEQ5P6762020  121 EHHSDHDHHSHHNHAASGKNKRKALCPDHDSDSSGKDPRNSQGKGAHRPEHASGRRNVKD 180
CG56008-04    118 -----S------------------------------------------------------ 118

SEQ5P6762020  181 SVSASEVTSTVYNTVSEGTHFLETIETPRPGKLFPKDVSSSTPPSVTSKSRVSRLAGRKT 240
CG56008-04    118 ------------------------------------------------------------ 118

SEQ5P6762020  241 NESVSEPRKGFMYSRNTNENPQECFNASKLLTSHGMGIQVPLNATEFNYLCPAIINQIDA 300
CG56008-04    118 ------------------------------------------------------------ 118

SEQ5P6762020  301 RSCLIHTSEKKAEIPPKTYSLQIAWVGGFIAISIISFLSLLGVILVPLMNRVFFKFLLSF 360
CG56008-04    118 ------------------------------------------------------------ 118

SEQ5P6762020  361 LVALAVGTLSGDAFLHLLPHSHASHHHSHSHEEPAMEMKRGPLFSHLSSQNIEESAYFDS 420
CG56008-04    119 ---------------D-------------------------------------------- 119

SEQ5P6762020  421 TWKGLTALGGLYFMFLVEHVLTLIKQFKDKKKKNQKKPENDDDVEIKKQLSKYESQLSTN 480
CG56008-04    119 ------------------------------------------------------------ 119

SEQ5P6762020  481 EEKVDTDDRTEGYLRADSQEPSHFDSQQPAVLEEEEVMIAHAHPQEVYNEYVPRGCKNKC 540
CG56008-04    119 ------------------------------------------------------------ 119

SEQ5P6762020  541 HSHFHDTLGQSDDLIHHHHDYHHILHHHHHQNHHPHSHSQRYSREELKDAGVATLAWMVI 600
CG56008-04    120 ------------------------------HHPHSHSQRYSREELKDAGVATLAWMVI 147

SEQ5P6762020  601 MGDGLHNFSDGLAIGAAFTEGLSSGLSTSVAVFCHELPHELGDFAVLLKAGMTVKQAVLV 660
CG56008-04    148 MGDGLHNFSDGLAIGAAFTEGLSSGLSTSVAVFCHELPHELGDFAVLLKAGMTVKQAVLV 207

SEQ5P6762020  661 NALSAMLAYLGMATGIFIGHYAENVSMWIFALTAGLFMYVALVDMVPEMLHNDASDHGCS 720
CG56008-04    208 NALSAMLAYLGMATGIFIGHYAENVSMWIFALTAGLFMHVALVDMVPEMLHNDASDHGCS 267

SEQ5P6762020  721 RWGYFFLQNAGMLLGFGIMLLISIFEHKIVFRINF                          755
CG56008-04    268 RWGYFFLQNAGMLLGFGIMLLISIFEHKIVFRINF                          302
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